

### Applicants' Contribution to the Art

Applicants' claims are directed to a method of preparing triple-layered microcapsules containing an enzyme stabilized therein by dispersing an enzyme into a low molecular weight polyol whose molecular weight is 1,000 g/mol or less to stabilize the enzyme, re-dispersing the dispersed enzyme/polyol solution into a polymer solution containing high molecular weight polyol whose molecular weight is more than 1,000 g/mol, and emulsifying the solution to prepare polymer microcapsules. A key feature of the present invention lies in using the low molecular weight polyol and high molecular weight polyol together, thereby the enzyme can be stabilized in the polymer.

Specifically, the enzyme is firstly stabilized by the low molecular weight polyol; the high molecular weight polyol acts as buffer that prevents direct contact between the enzyme and the hydrophobic polymer wall material in the microcapsule. After that, the aqueous solvent is removed and thus a phase separation is formed, and during this separation, the low molecular weight polyol flows out to the outer aqueous phase through an external interface of the microcapsule, due to its high polarity, and high molecular weight polyol remains in the microcapsule. At the conclusion of the process, the microcapsule is composed of triple layers in which the enzyme forms the internal core, hydrophobic high molecular weight polyol surrounds the enzyme, and finally the wall-component polymer forms the outer wall (*see* pages 9-10 of the specification). Neither of the applied references disclose these technical features.

### Response to Rejection

The sole issue raised in the outstanding Official Action is the patentability of claims 12 and 19 and whether they are "obvious" over the combined disclosures of WO 00/32307 to Mathiowitz in view of U.S. patent 5,672,213 to Asgharian et al.

After providing a brief synopsis of the thought-to-be-relevant passages of the primary reference in items 4-8, the Official Action acknowledges that the primary reference "teaches all of the claim limitations with the exception of dispersion of the enzyme into a low molecular weight polyol". For this reliance is placed on the Asgharian reference which is said to disclose "the stabilization of enzymes prior to use in order to obtain maximal activity once the enzyme is put to use ... Specifically, the Asgharian reference discloses the use of polyols to aid in stabilization of the enzyme" and then goes onto specify various types of polyols. Unfortunately,

the Official Action does not comment on or take into account the complete content of the applied reference. These may be conveniently found, for instance, in the following passages.

“The liquid enzyme compositions of the present invention contain critical amounts of selected stabilizing agents. The stabilizing agents utilized are combinations of an aromatic acid derivative and at least one polyol.” [Column 3, lines 6-9.]

“The compositions of the present invention contain an aromatic acid derivative and a polyol to stabilize the enzymes in an aqueous medium. It has surprisingly been found that aromatic acids are efficacious in inhibiting enzymes in liquid enzyme compositions.” [Column 3, lines 56-60.]

“...it is believed that the stability of these enzymes is enhanced by inhibiting the enzymes prior to use. Aromatic acid derivatives inhibit the enzyme by both electrostatically and hydrophobically binding the enzyme.” [Column 3, lines 62-65.]

“... the use of an aromatic acid derivative in combination with at least one polyol achieves the stability and sustainable activity required in the liquid enzyme compositions of the present invention.” [Column 4, lines 8-11.]

From the above quotations as well as the overall import of the applied reference itself one will clearly have the understanding that the polyol by itself is not disclosed as being effective to stabilize the enzymes. In fact, it is clearly the combination of the polyol and “an aromatic acid derivative” of the type specified, for instance, in the discussion beginning at column 4, line 13 and onward that is essential to achieve stabilization.

It is inappropriate to apply this reference for less than it fully teaches and requires. In fact, polyols are mentioned but not by themselves. One having ordinary skill in this art would not select either a polyol or one of the aromatic acid derivatives by itself in order to seek stabilization of an enzyme and expect to obtain useful results, but that is exactly what the Official Action does.

Critical information present in the reference is not acknowledged in the Official Action and has not been taken into account when assessing claims 12 and 19 for patentability, specifically non-obviousness. The art does not provide a teaching of using a polyol by itself on

the basis of the applied reference. In fact, it is quite the opposite that two components are required to satisfy the degree of stabilization the reference requires and there is no motivation or suggestion to one skilled in the art to use one of the two components independent of the other. Withdrawal of the rejection and allowance of claims 12 and 19 is in order.

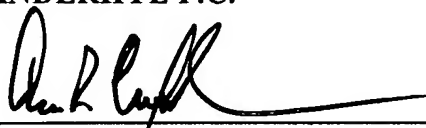
Information Disclosure Statement

With respect to the Information Disclosure Statement earlier submitted, apparently the examiner requests a listing of the communication from the European Patent Office. A new Information Disclosure Statement is filed herewith which includes the appropriate listing and the relevant fee has been paid. The examiner is requested to peruse the content of the document attached with the concurrently filed Information Disclosure Statement and to acknowledge consideration of same for which applicants have paid a fee.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_



Arthur R. Crawford

Reg. No. 25,327

ARC:eaw  
901 North Glebe Road, 11th Floor  
Arlington, VA 22203-1808  
Telephone: (703) 816-4000  
Facsimile: (703) 816-4100